IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Examiner: Saoud, Christine J.
Avi J. ASHKENAZI, *et al.*	)	Art Unit: 1647
Application Serial No. 10/016,177	)	Confirmation No: 4438
Filed: October 25, 2001	)	Attorney's Docket No. 39780-2630 P1C90
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	)	**Customer No. 35489**

DECLARATION OF KEVIN P. BAKER, Ph.D., AUDREY GODDARD, Ph.D., PAUL J. GODOWSKI, Ph.D., AUSTIN GURNEY, Ph.D., DANIEL TUMAS, Ph.D. AND WILLIAM I. WOOD, Ph.D. UNDER 37 C.F.R. §1.131

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

We, Kevin P. Baker, Ph.D., Audrey Goddard, Ph.D., Paul J. Godowski, Ph.D., Austin Gurney, Ph.D., Daniel Tumas, Ph.D. and William I. Wood, Ph.D. declare and say as follows:

1. We are the inventors of the above-identified application.

2. We have read and understood the claims pending in this application, and are aware that the claims have been rejected as anticipated by U.S. Patent No. 6,610,286 (Thompson et al., published August 26, 2003, with priority to December 23, 1999) and by U.S. pre-grant publication No. 20030175778 (Ni et al., published September 18, 2003 with priority to June 5, 1998).

3. The polypeptide designated as PRO1114 (SEQ ID NO:352) claimed in the above-identified application in the United States was sequenced and cloned and homology to cytokine receptor family proteins identified prior to June 5, 1998.

4. U.S. Provisional Application Serial No. 60/087,106, filed on May 28, 1998, discloses sequences designated as SEQ ID NO:1 and SEQ ID NO:3, which are identical to SEQ ID NO:351 and SEQ ID NO:352, respectively, of the above-identified application.

5. U.S. Provisional Application No. 60/087,106 further discloses that PRO1114 corresponding to SEQ ID NO:352 is a cytokine receptor family protein.

6. We conceived and reduced to practice the invention claimed in the above-identified application in the United States prior to June 5, 1998.

7. At the time the present invention was made, one of the inventors, Daniel Tumas, Ph.D., was, as still is, responsible for overseeing the testing of novel polypeptides, including the polypeptide designated PRO1114, in an assay of inhibitory activity in the mixed lymphocyte reaction (MLR) (Assay #67, Example 130). This assay is used to find agents that are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

8. The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO_2) and then washed and resuspended to $3x10^6$ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:l of test sample diluted to 1% or to 0.1%,

50 :l of irradiated stimulator cells, and

50 :l of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO_2 for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to $1x10^7$ cells/ml of assay media. The assay is then conducted as described above.

Any decrease below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein. The results are indicative of the utility of the PRO polypeptides in therapeutic applications where suppression of an immune response is beneficial.

9. Copies of pages from an internal database showing the positive results for the PRO1114 polypeptide (SEQ ID NO:352), identified by Pin number PIN620-1, in Assay #67 are attached to this declaration (with dates redacted) as Exhibit A. These experiments were performed and the results were obtained in the United States prior to December 23, 1999.

10. Exhibit A clearly shows that the polypeptide designated PRO1114 was tested, and its ability to inhibit the mixed leukocyte reaction was determined prior to December 23, 1999.

11. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information or belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Kevin P. Baker, Ph.D.	Date
Audrey Goddard, Ph.D.	Date
Paul J. Godowski, Ph.D.	Date
Austin Gurney, Ph.D.	Date
Daniel Tumas, Ph.D.	Date
William I. Wood, Ph.D.	Date

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